REMARKS

Attached hereto is a marked-up version of the changes made to the Specification by the current amendment. The attached page is captioned "Version with markings to show changes made."

Claims 1, 18-20 and 26-32 are pending in the application. Claims 27-32 have been withdrawn from consideration. Claims 1, 18-20 and 26 are actively being prosecuted.

Applicants have presented evidence as seen in Exhibits A-K filed with the Response of October 17, 2002, the ClustalW alignment faxed to Examiner Davis on January 28, 2003, the Preliminary Amendment filed January 21, 2003, and the Supplemental Preliminary Remarks requested by Examiner Davis, faxed March 19, 2003, that HPAK shares homology with the kallikrein gene family, a family consisting of members known to have undisputed utility, functioning as protease enzymes. Applicants have also provided in the Supplementary Preliminary Remarks extensive explanations of selected Exhibits submitted October 17, 2002, including their findings and interpretation of evidence disclosed, in support of the utility of HPAK. Applicants continue to assert that their submitted evidence substantiates that HPAK belongs to the kallikrein gene family, and thus, is useful as a serine protease enzyme molecule.

Objection

Claim 26 was objected to as drawn to the same composition as claim 20. Claim 26 has been canceled. Thus, the objection is rendered moot.

Utility Rejections under 35 U.S.C. § 101 and § 112, first paragraph

Applicants wish to express their appreciation to Examiner Davis and Supervisory Primary Examiner Caputa for clarifying the outstanding rejections in the instant application during the phone interview of May 6, 2003. Applicants' representatives were left with the impression following the interview that Examiner Davis acknowledged that Applicants' invention was the polypeptide comprising

the amino acid sequence of the kallikrein 11 protein, a serine protease enzyme molecule and, thus, the rejection for lack of utility and enablement due to a lack of utility would be withdrawn.

Applicants bring to the Examiner's attention that the kallikrein 11 protein has 90% sequence identity to SEQ ID NO:1 and, thus, falls within the scope of the instant invention as claimed. Thus, Applicants' invention includes the kallikrein 11 protein, the sequence of which falls within the claim language of claim 1. Therefore, Applicants request reconsideration and withdrawal of the rejections of claims 1, 18-20 and 26 under 35 U.S.C. § 101 and § 112, first paragraph.

Scope of Enablement Rejections under 35 U.S.C. § 112, first paragraph

Claims 1(b), 20 and 26 were also rejected under the first paragraph of 35 U.S.C. §112 because the Specification allegedly did not provide an enabling disclosure commensurate in scope with the claims. This rejection is traversed.

The Office Action has asserted, *inter alia*, that "SEQ ID NO:1 has not been convincingly demonstrated to be a serine protease" (Office Action of April 10, 2003, page 22). Applicants' representatives reiterate that during the interview of May 6, 2003, Examiner Davis was convinced that Applicants had indeed discovered the kallikrein 11 protein, known to one of skill in the art to have serine protease activity. Thus, this matter should no longer be at issue.

The Office Action has also asserted, *inter alia*, that claims 1, 20 and 26 read on naturally-occurring allelic variants of SEQ ID NO:1. The Office continues:

> Thus the scope of the claims includes numerous structural variants that would exist in nature. No common structural attributes that identify the claimed variants are disclosed, because the function of SEQ ID NO:1 has not been convincingly demonstrated to be a serine protease . . . (Office Action of April 10, 2003, page 23).

Note, however, that SEQ ID NO:1 has been convincingly demonstrated to be a serine protease. Common attributes of serine proteases include signal sequences important for kallikrein secretion at the amino terminus, the conserved residues H_{65}, D_{113}, and S_{206} for serine protease activity, and 10 conserved cysteine residues (at positions 31, 50, 66, 145, 166, 177, 191, 202, 212, and 227) which are involved in the formation of five disulfide bonds. All of the aforementioned are common structural

attributes and contribute to the common function of SEQ ID NO:1 variants as having serine protease activity. See the Specification, for example, at page 11, lines 8-17, and Figures 2A and 2B. Moreover, the Specification provides an assay for the determination of HPAK proteolytic activity (Example IX, page 44).

Given the information provided by SEQ ID NO:1 (the amino acid sequence of HPAK) and the common structural attributes and common functional attributes used to identify the claimed variants, one of skill in the art would be able to routinely obtain variants of the SEQ ID NO:1 polypeptide having serine protease activity commensurate in scope with the claims.

The Office Action has also asserted, *inter alia*, that the Specification provides insufficient guidance for one of skill in the art to "obtain naturally-occurring allelic variants of SEQ ID NO:1" (Office Action of April 10, 2003, page 22). Note, however, that the claims recite not only that the polypeptides have at least 90% sequence identity to SEQ ID NO:1, but also have "***a naturally-occurring amino acid sequence***." Through the process of natural selection, nature will have determined the appropriate amino acid sequences.

Given the information provided by SEQ ID NO:1 (the amino acid sequence of HPAK) and SEQ ID NO:2 (the polynucleotide sequence of HPAK), one of skill in the art would be able to routinely obtain "a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the sequence of SEQ ID NO:1 over the entire length of SEQ ID NO:1, said polypeptide having serine protease activity." For example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the Specification of the instant application. See, *e.g.*, page 33, lines 10-22; and Example VI at page 43. Thus, one skilled in the art need not make and test vast numbers of polypeptides that are based on the amino acid sequence of SEQ ID NO:1. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides/polypeptides that already exist in nature.

Accordingly, the Specification would allow one of skill in the art to practice the full scope of what is claimed. Withdrawal of this rejection is therefore requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent at (650) 621-8555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE CORPORATION

Date: 10, July 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 26 has been canceled.